Bandolier 138

Independent evidence-based thinking about health care

On being eclectic

Bandolier revels in eclecticism, finding material from different sources. So many questions to ask and such a lot to find. Questions come from readers (whiplash and soft collars, and probiotics for pouchitis in this issue), from topics covered previously (aspirin and cancer), from stuff found by accident (click to be sick?), and things that have interested us before and niggle (honey for wounds, and anaemia).

What constitutes evidence is another driver, because it varies so much. Most of us would usually tend to dismiss evidence from a few tiny trials, but when there is a very large effect from high quality, valid trials of long duration, tiny trials can still be compelling (pouchitis).

Difficult topics

It is rarely this easy, though. Take honey and wounds. We have a clutch of trials of limited quality, and even a systematic review, but despite some biological plausibility we tend to hang back. Yet there is power in case reports and case series. When a case of almost miraculous recoveryis reported in impossible circumstances we should take notice. We should also ask why, given impressive results, good trials are not being done to convince us.

The answer is that there is little or no commercial interest - can any of us really expect to see our favourite supermarket sponsoring a trial? But when even a casual glance indicates possible big benefits to healthcare providers, it seems strange that none can get organised to investigate this for their own (and our) benefit.

Anaemia is another difficult topic. Bandolier has had an interest in this for a while, but it has taken time get a grip on it. Anaemia is clearly bad news, especially in sick older people. But the subject is so multifactorial that understanding it will take time.

And finally, a warning about the power of the press release is chilling.

In this issue

Anaemia and mortality in older people

Bandolier 137 examined a systematic review of the prevalence of anaemia in older people, and noted that prevalence increased with age, and was rather high. What was not clear was any relationship between anaemia and any other consequences. Anaemia was associated with higher rates of Alzheimer's disease, poorer health, more hospital admission, and greater mortality, though none of the studies reporting this was large. A further search has found more information from three studies relating anaemia, heart failure, kidney failure, and mortality.

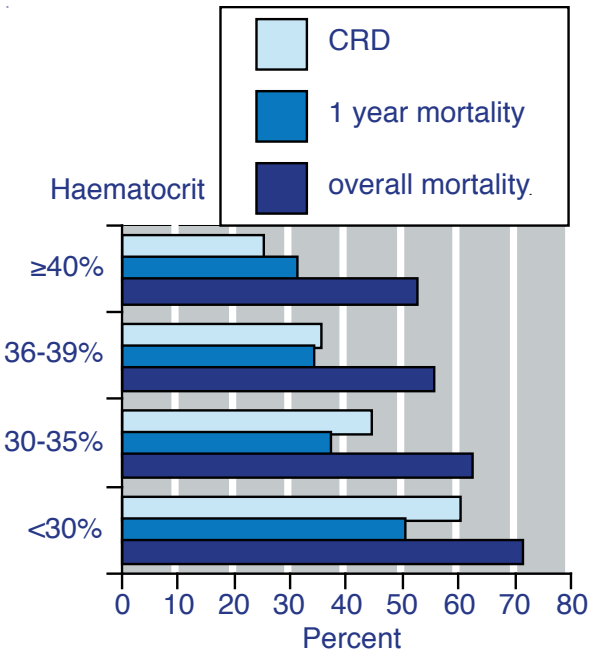
Admission with heart failure [1]

The population was all Medicare patients admitted in a US state over six months with a primary diagnosis of heart failure. Retrospectively information from patient records was abstracted, with follow up over more than two years.

Results

After excluding patients with frank renal failure, who died before discharge, or who were lost to follow up, 665 such patients were eligible. Their average age was 76 years, with a range of 29 to 100 years. Multiple conditions were recorded

Figure 1: Chronic renal disease, and one year and 2.5 year mortality with haematocrit in older patients with heart failure



including hypertension, diabetes, coronary artery disease, myocardial infarction, stroke, and angina. With decreasing haematocrit, the proportion with chronic renal disease, or who died within the first year, or 2.5-year mortality, increased significantly (Figure 1).

Anaemia predicts mortality in heart failure [2]

Baseline and follow up data from a randomised trial of amlodipine versus placebo in 1,130 patients with severe heart failure were used. Average age was 65 years. Follow up was over 15 months, and there were 407 deaths, predominantly cardiac deaths. Patients were divided into quintiles according to their baseline haematocrit. The lowest quintile had a haematocrit of <38% and haemoglobin of 116 g/L.

Results

In the lowest quintile total mortality was 41%, compared with 25-28% across other quintiles. It was significantly higher, with a hazard ratio of 1.5 (1.1 to 2.1) adjusting for a range of factors. In this lowest quintile each 1% fall in haematocrit was associated with an 11% higher risk of death.

There was a strong effect of haematocrit across all quintiles for pump failure death (Figure 2), with significant increased risk in all four lower quintiles compared with the highest quintile. There was no effect on sudden or other deaths.

Myocardial infarction [3]

Another retrospective cohort study randomly selected 15% of patients discharged from hospital with the primary diagnosis of acute myocardial infarction in a single US state. Follow up was over 2.5 years.

Results

After obvious exclusions, information from 559 patients was available. The average age was 74 years, ranging from 32 to 97 years. As haematocrit on admission fell from 40% to under 30%, the prevalence of chronic renal disease rose from 48% to 80%, and one-year mortality from 19% to 42%. Low creatinine clearance and low haematocrit were independent

Figure 2: Pump failure deaths over 15 months and baseline haematocrit in patients with severe heart failure

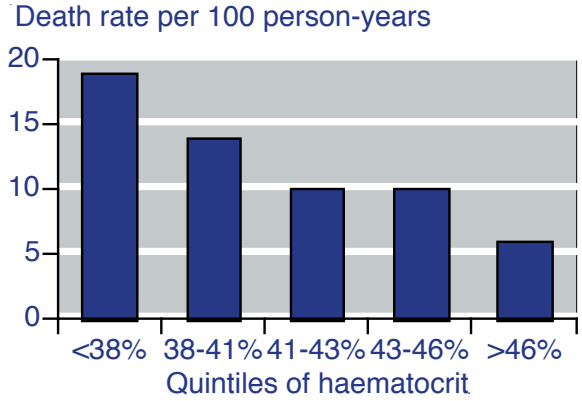
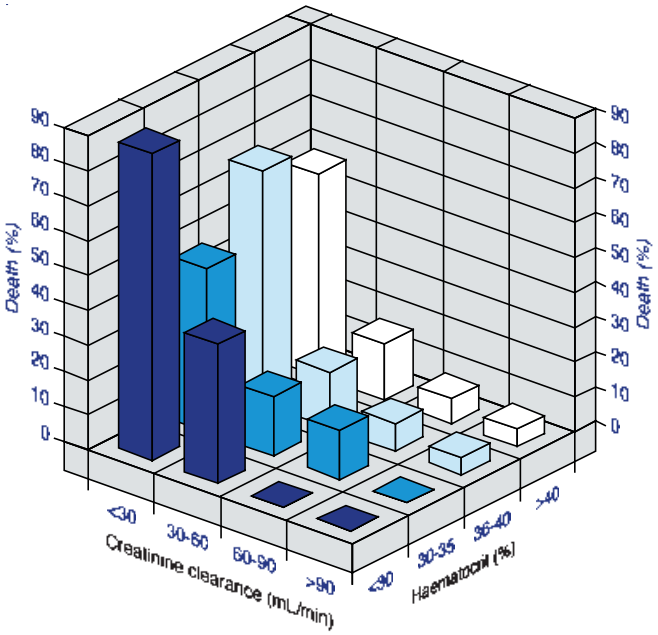


Figure 3: One-year mortality after myocardial infarction according to haematocrit and creatinine clearance



risk factors for risk of death within one year. The risk was very high with both factors (Figure 3).

Comment

Chronic anaemia is known to have effects on the heart, increasing heart rate and how much the heart has to work. That's obvious, because if the body demands a certain amount of oxygen, but the oxygen carrying capacity of the blood is reduced, more blood has to be pumped in a given time. The heart is stressed.

The relationship between renal failure and anaemia is complex, especially as regards causation. Renal failure may contribute to anaemia, but anaemia may also contribute to renal impairment. Both anaemia and renal impairment may be also be caused by some other factor that is itself a cause of increased mortality.

What we do not know is whether treating the anaemia does any good. So far there is little to help, but the question of transfusion for anaemia after a heart attack is tiger territory, with studies pointing to different conclusions. What we are left with for the moment is a few stark facts. Anaemia is not a good thing in older people with heart failure or heart attack. Nor is renal insufficiency. Having both is very bad.

References:

1 WM McLennan et al. Anemia and renal insufficiency are independent risk factors for death among patients with congestive heart failure admitted to community hospitals: a population-based study. Journal of the American Society of Nephrology 2002 13: 1928-1936.

2 D Mozaffarian et al. Anemia predicts mortality in severe heart failure. Journal of the American College of Cardiology 2003 41: 1933-1939.

3 RD Langston et al. Renal insufficiency and anemia are independent risk factors for death among people with acute myocardial infarction. Kidney International 2003 64: 1398-1405.

Soft collars for whiplash – Bandolier review

Rear impact road traffic accidents are no joke, as Bandolier discovered recently in a misunderstanding with a 40-tonne truck on the M25 around London. One feature is that some people have a soft tissue sprain to the neck, often called a whiplash injury. These are often treated with a soft collar to partially immobilise the neck. A Bandolier reader asked about the evidence for their effectiveness.

Systematic review

Bandolier sought randomised trials comparing soft collars with any other therapy, or no therapy, published in the last 10 years or so. The choice of last 10 years was to minimise any change in soft collar design that may have taken place. It was unlikely that such trials would be blind, and all would likely have low quality scores, so quasi-randomised trials were also accepted.

Any useful outcome was acceptable, but those of greatest interest were pain, time off work, or outcome relating to recovery, at any time after the injury.

Results

Five trials were found (Table 1). Two were quasi-randomised, and two had six-week outcomes. Others had longer outcomes, between six months and three years. Six month or one year outcomes were chosen. Most of the studies used a whole series of outcomes, mostly including pain, but also time off work and other measures. Each had some dichotomous outcome equating to a treatment success, such as no or lower level pain, or no symptoms, or global improvement.

Analysis of these dichotomous outcomes is shown in Figure 1 and Table 1. In the two trials where the control was no other treatment, soft collars were no better, with a relative risk for a successful outcome of 1.0 (0.9 to 1.2).

Exercise and early mobilisation, the control in three trials, were superior to soft collars, producing higher success rates. In these three trials the success rate was only 58% with soft collars, compared with 70% with exercise (Table 2). Using a soft collar instead of exercise would result in a statistically poorer result, with a relative risk of 0.82 (0.69 to 0.97), and a number needed to harm of 9 (4 to 142). For every nine patients with whiplash, one would have a poorer outcome if treated with a soft cervical collar.

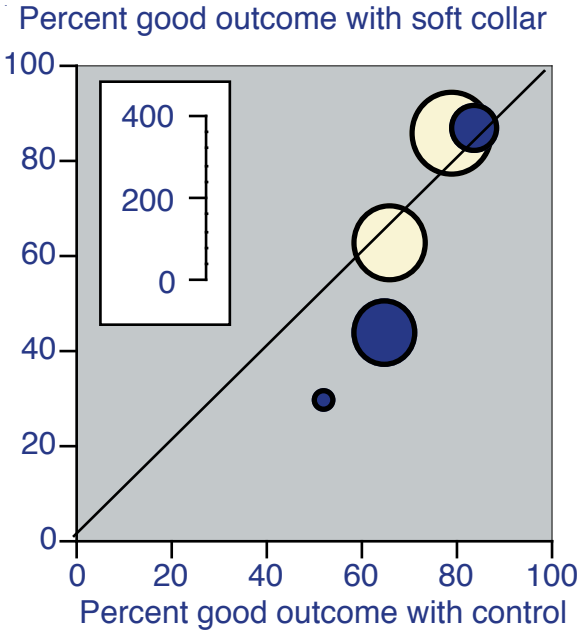
Table 1: Randomised or quasi-randomised trials comparing soft collars with no-treatment or other controls for neck strain after motor vehicle accident

Reference	Design	Patients	Outcomes	Results
Gennis et al. Academic Emergency Medicine 1996 3: 568-573	Quasi-randomised (record number). Soft collar to be worn for as much as possible for first two weeks No treatment Both groups advised to rest and use NSAIDs	All patients with neck pain within 24 hours of motor vehicle collision	Six-week report of pain by telephone call 250 patients enrolled, 196 providing data	No pain or better in: 89/104 soft collar 73/92 in control
Borchgrevink et al. Spine 1998 23: 25-31	Random assignment to: soft collar and 14 days sick leave act as usual without sick leave	Patients with neck sprain caused by car accident, aged 18-70 years	Range of outcomes at six months, including pain in a variety of circumstances, ear symptoms, headache. 201 recruited, with 23 not reporting at six months	Global improvement of fewer symptoms 60/96 soft collar 54/82 act as usual Significantly better for act as usual for subjective symptoms, pain, and headache
Rosenfeld et al. Spine 28 22: 2491-2498	Randomised to: soft collar and written advice exercise programme based on early and repeated movement	Consecutive patients exposed to whiplash trauma in motor vehicle accidents	Range of outcomes at six months and three years. 44 reported who received early intervention in first 96 hours	Low level pain at 6 months: 7/23 soft collar 11/21 active exercise Low pain at 3 years: 9/21 soft collar 7/18 active exercise Active exercise patients had considerably less sick leave over three years
Schnabel et al. Emergency Medicine Journal 2004 21: 306-310	Randomised to: soft collar for one week, advised to wear continuously instruction from physiotherapist on exercises and mobilisation	Patients with pain, stiffness or numbness in spine head or limbs within 48 hours of motor vehicle collision, at least 18 years old	Range of outcomes at six weeks. 200 patients randomised; withdrawals 36% of collar group and 15% physiotherapy group	No symptoms at six weeks (per protocol): 27/62 collar 57/88 exercise No symptoms at six weeks (ITT): 27/97 collar 57/103 exercise Exercise group had significantly less pain in neck, and shoulder, and fewer had headaches
Crawford et al. Injury 2004 35: 891-895	Initial treatment with soft collar and NSAIDs, then at clinic randomised (record number) to: soft collar for 3 weeks then mobilised or early mobilisation without collar	All patients in road traffic accident with neck pain within 48 hours of injury, over age 18 years	Activities of daily living, pain, and range of movement at 3, 12 and 52 weeks	At one year, patients with normal level of function: 46/53 collar 46/55 mobilisation

Table 2: Results of trials of soft collar for whiplash, using patients with good outcome at six months or one year

Comparator	Number of Trials	Number of Patients	Percent good outcome Collar	Percent good outcome Control	Relative risk (95% CI)	NNH (95% CI)
No active treatment	2	374	75	73	1.0 (0.9 to 1.2)	not applicable
Exercise	3	302	58	70	0.82 (0.69 to 0.97)	9 (4 to 142)
All trials	5	676	68	71	0.9 (0.8 to 1.1)	not applicable

Figure 1: Soft collar trials; dark symbols have exercise controls, light symbols no treatment



Comment

Soft collars look like a waste of time. Though Bandolier limited its search to recent studies, older trials and observational studies seem to be in agreement: soft cervical collars probably do less good than giving people exercises.

A shame then that they are still used. A survey of recent Welsh practice [1] showed that half of all grades of medical staff in accident and emergency units would use soft collars for whiplash injuries. Advice on exercise was usually given, always by consultants. Physiotherapy was rarely used, though more often by consultants. Staff with greater experience made more appropriate decisions.

For whiplash injuries, soft collars, for most people, are not worth having, and may do less good than exercise.

Reference:
1 AJ Logan, MD Holt. Management of whiplash injuries presenting to accident and emergency departments in Wales. Emergency Medicine Journal 2003 20: 354-355.

Honey for wounds

In 2001 Bandolier online featured a systematic review [1] of honey and wounds, together with a follow up including two more randomised trials. These have prompted more than their fair share of attention through emails and other contacts, so a brief re-visit makes sense. Disappointingly, there is little more of note to report.

Honey has been used to treat infected wounds and burns. There is logic to this because it is hyperosmolar, and because it contains specific antimicrobial substances. Trials have been randomised, but usually of low reporting quality otherwise, and predominantly from a single researcher. Healing of burns at seven days was higher with honey (48%) than active controls (16%, Figure 1), with an NNT of 3.1 (2.5 to 4.2).

Case series in venous leg ulcers [2]

A case series without controls recruited 40 patients with predominantly venous leg ulcers which had failed to respond to a minimum of 12 weeks of appropriate treatment with compression bandaging following appropriate guidelines. There were also sensible exclusions, like concomitant use of antibiotics, ulcers larger than 18 x 8 cm, an ulcer present for more than two years, or an inability of carers to change dressings.

Treatment was with medihoney (an Australian antibacterial honey) spread to a depth of about 3 mm and to the shape of the ulcer, with compression bandage, though how often wasn't stated. Pain, healing, wound size, and odour were monitored over a further 12 weeks.

Table 1 shows some of the results. There were 13 withdrawals, eight because of increased pain or worsening ulcer. On the other hand, 20 patients who had pain initially had their pain much reduced. Pain appeared to be related to the size of the leg ulcer.

Of the 27 patients who remained in the study, seven had wounds healed by 12 weeks, and 20 had a reduction in wound size. Six, though, had also received oral antibiotics. Odour was present in 26 patients, and odour scores dropped during the study, from an average mild/moderate odour to average no odour/mild odour. Only seven of 40 patients were less satisfied with the honey than with previous treatment.

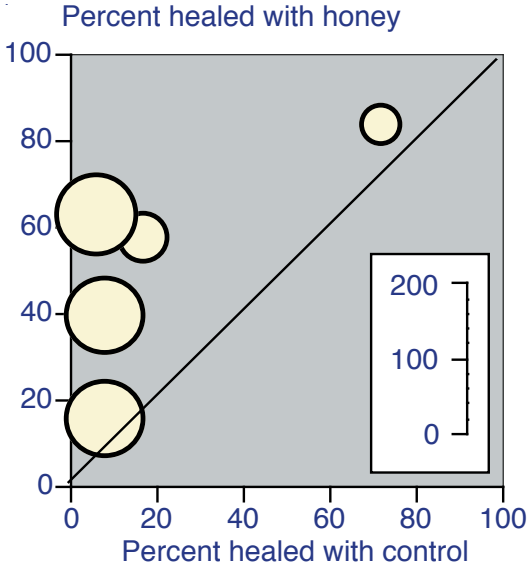
Case report of a diabetic foot ulcer [3]

Here a 79-year old man had diabetic heel and forefoot ulcers, which were treated over 14 months, including five hospital

Table 1: Results of a case series of 40 patients with predominantly venous leg ulcers, unhealed after 12 weeks of compression bandaging using standard guidelines

Outcome	Number	Comment
Started	40	Age 54-96 years, 90% venous ulcers, average size 10 sq cm, range 0.2 to 61 sq cm after 12 weeks of compression therapy according to local and national guidelines
Withdrew	13	Increasing ulcer pain (6), poor health (3), deteriorating ulcer (2), death (1), not treated to protocol (1)
Pain decreased	20	From average initial of discomfort (moderate pain) to almost no pain, and average wound area from 8 to 4 sq cm
No pain initially	4	Average wound area decreased from 3 to 2.4 sq cm
Pain increased (including dropouts)	11	Pain increased from slight/discomfort to discomfort/distressing. Average wound area increased from 12 to 13 sq cm

Figure 1: Healing of burn wounds at seven days with honey compared with active controls



admissions and four operations (with loss of several toes). The ulcers measured 8 x 5 and 3 x 3 cm, and were infected with MRSA, VRE (vancomycin-resistant Enterococcus), and Pseudomonas. The cost of his ulcer treatment over the 14 months was US$390,000.

Refusing amputation, the patient was discharged home. The wounds were smeared with ordinary honey from a supermarket, and then wrapped. No oral antibiotics were used.

Within two weeks granulation tissue appeared, and within a year the ulcers were healed. Two years later the man was ambulatory with a walker.

Comment

The importance of case reports in relation to adverse events with drug has recently been eloquently emphasised [4]. Case reports with treatments can also be compelling. Here we have two forms of anecdotal evidence, which can be placed in the scales.

The case series was a non-comparative trial on patients who had failed to respond to conventional therapy, but where a majority appeared to respond well to honey. After 12 weeks of honey they had reduced pain, reduced odour, and ulcers that began to heal or had healed. We cannot know whether 24 weeks of compression therapy would have done as well as 12 weeks of compression plus 12 weeks of compression and honey, and therein is the weakness of a case series.

Perhaps the case report is more convincing. This patient had everything stacked against him. A long period of ineffective treatment, ulcers infected with some very nasty resistant bugs, and the best medical advice urging amputation. Honey helped within a couple of weeks. Here causation seems plausible.

We have biological plausibility that honey should be effective. It comes from knowledge that its hyperosmolar nature and antibiotics should help. Randomised trials show that it does help, even though those trials had weaknesses. Case series and reports add to evidence.

What is disappointing is that in the four years or so since the systematic review, no major randomised trials have been published to help us decide who to treat, with what, when, and for what condition. This is curious when there is an apparently relatively simple, low-tech solution to some frightening, costly problems. Our health service and academic institutions seem too sclerotic to organise effective clinical research.

References:

1 OA Moore et al. Systematic review of the use of honey as a wound dressing. BMC Complementary and Alternative Medicine 2001 1: 2. (http://www.biomedcentral.com/1472-6882/1/2)
2 CE Dunford, R Hanano. Acceptability to patients of a honey dressing for non-healing venous leg ulcers. Journal of Wound Care 2004 13: 1-7.
3 JJ Eddy, MD Gideonson. Topical honey for diabetic foot ulcers. Journal of Family Practice 2005 54: 533-536.
4 JK Aronson. Unity from diversity: the evidential use of anecdotal reports of adverse drug reactions and interactions. Journal of Evaluation in Clinical Practice 2005 11: 195-208.

Probiotics for pouchitis

Pouchitis is a non-specific acute inflammation within an ileal reservoir. It leads to increased frequency of loose stool, and abdominal cramping. About half of people having surgery, usually for ulcerative colitis, have at least one episode of pouchitis over about 10 years. Treatment is usually with antibiotics, but a minority of patients (perhaps 10%) experience refractory or frequently recurrent pouchitis, usually regarded as two episodes or more in a year. Even so, antibiotics can be effective.

The problem is in maintaining a pouchitis-free state thereafter. Probiotics have been suggested as being helpful, and this brief Bandolier review examines the evidence.

Search

Bandolier sought randomised trials for the use of probiotics in pouchitis. There was no prior intent to differentiate between different probiotics, for any specific outcome in trials, or type of pouchitis.

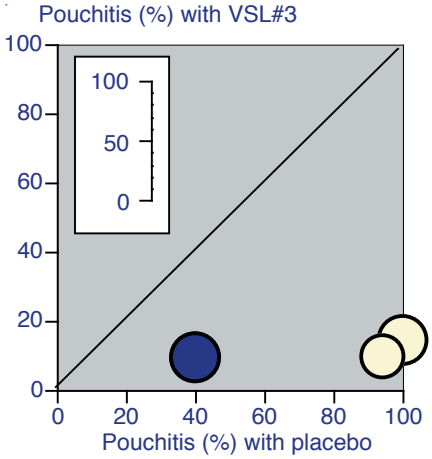
Results

Four randomised trials were found. Three concerned VSL#3, containing four strains of lactobacilli, three strains of bifidobacteria, and one strain of streptococcus salivarius. This was presented in bags with about 300 billion bacteria per gram. One trial concerned use of lactobacillus GG, in a formulation of about 10 billion bacteria per capsule. These were analysed separately.

VSL#3

The trial details are shown in Table 1. Two of them were for prophylaxis against pouchitis in patients with established refractory or frequently recurrent pouchitis, and one was in patients without pouchitis, as prophylaxis against it developing.

Figure 1: Incidence of pouchitis with VSL#3 and placebo over 12 months (open symbols secondary, filled symbols primary prevention)



The duration of trials was nine or 12 months. The three trials were of good reporting quality (generally scores of 3 to 5 out of 5 on a popular scoring system), but were small, with about 40 patients in each. Patients had 600 to 900 billion bacteria daily.

Results were good, with low rates of pouchitis with VSL#3, but high rates with placebo, the common comparator (Figure 1). Overall there was a big reduction with VSL#3, with relative risk of developing pouchitis of 0.2 (95% confidence interval 0.1 to 0.3). The number needed to treat to prevent pouchitis was 1.5 (1.3 to 2.0).

In those with refractory or frequently recurrent pouchitis, placebo pouchitis rates were almost 100%, but were about 10% with VSL#3. The number needed to treat to prevent pouchitis over about a year was 1.2 (1.0 to 1.4).

One adverse event was noted on VSL#3. One patient had abdominal cramps, vomiting, and diarrhoea on VSL#3, recurring on repeat challenge.

Table 1: Randomised trials of VSL#3 versus placebo for pouchitis

Reference	Design	Patients	Outcomes	Results
Gionchetti et al. Gastroenterology 2000 119: 305-309	Randomised, double blind, placebo controlled, parallel group comparison of VSL#3 with placebo over 9 months; 20 patients in each group Oral 3 g bags twice daily	Adults (18-65 years) with chronic relapsing pouchitis of at least 3 relapses per year, in clinical and endoscopic remission	Relapse, defined as at least 2 point increase in clinical portion of specific disease activity index, confirmed by endoscopy or histology	Patients were well matched at baseline Relapses in: 20/20 on placebo (all by 4 months) 3/20 on VSL#3 (all relapsed within 4 months of end of therapy) No adverse events noted
Gionchetti et al. Gastroenterology 2003 124: 1202-1209	Randomised, double blind, placebo controlled, parallel group comparison of VSL#3 with placebo over 12 months; 20 patients in each group Oral 3 g bag once daily	Adults (18-65 years). Randomisation was within 1 week of ileostomy closure	Episodes of acute pouchitis, defined as total disease activity score of 7/18 or more	Patients were well matched at baseline Acute pouchitis: 8/20 on placebo 2/20 on VSL#3 No adverse events noted
Mimura et al. Gut 2004 53: 108-114	Randomised, double blind, placebo controlled, parallel group comparison of VSL#3 with placebo over 12 months; 20 patients on VSL#3 and 16 on placebo Oral 6 g bags once daily	Patients with active refractory or recurrent pouchitis (disease score of 7 or above) in remission after antibiotic therapy	Relapse, defined as at least 2 point increase in clinical portion of specific disease activity index, confirmed by endoscopy or histology	Patients were well matched at baseline Relapses in: 15/16 on placebo (all by 4 months) 2/20 on VSL#3 (all relapsed within 4 months of end of therapy) One patient had abdominal cramps, vomiting, and diarrhoea on VSL#3, recurring on repeat challenge

Lactobacillus GG

One small trial involving 20 patients [1] treated previously for clinical symptoms of pouchitis randomised them into two groups, treated with either four capsules of lactobacillus GG a day (40 billion bacteria) or placebo for three months. It showed changed pouch intestinal bacterial flora in four subjects, but few other changes. Though most patients had pouchitis, only one patient in the lactobacillus group may have improved.

Comment

Numbers needed to treat below 2 are rare, so that the NNTs to prevent pouchitis with VSL#3 therapy should be taken seriously. Though numbers of patients were small, results were consistent in valid studies of reasonable reporting quality. Although acute pouchitis was the outcome concentrated on here, other useful results of interest to gastroenterologists were reported in the trials. It is an interesting example of small numbers of small trials properly done, where a big effect can be taken seriously.

Probiotic use in gastrointestinal diseases has been reviewed recently [2], though not with a systematic search. It suggests that treatment of acute diarrhoea in children and prevention of antibiotic associated diarrhoea are the only two areas with any likely utility. A review of the latter (Bandolier 104) suggested an NNT of only about 10, making the results for pouchitis much more impressive. One issue, though, is the range of bacteria, and the very high dose in the VSL#3 studies. Not all probiotics are the same.

References:
1 J Kuisma et al. Effect of lactobacillus rhamnosus GG on ileal pouch inflammation and microbial flora. Alimentary Pharmacology and Therapeutics 2003 17: 509-515.
2 A Sullivan, CE Nord. Probiotics and gastrointestinal diseases. Journal of Internal Medicine 2005 257: 78-92.

Low-dose aspirin and cancer

Past observational studies have noted a tendency for lower cancer rates in people who took aspirin or NSAIDs on a regular basis. On the basis of this, trials have been performed to see if aspirin, and, later, coxibs, prevented or delayed colorectal polyp development. The choice of colorectal polyps was because this was a surrogate marker of cancer prevention, in studies that could be done relatively quickly, over one to three years. The results were summarised in Bandolier 129, showing small effects if any.

Real clarity would only come from large, long-term studies, especially in primary prevention. Knowing the answer is important. In the USA in particular, much has been written in the media in recent months suggesting that an aspirin a day cures all known ills.

Not so, as we know that aspirin at any dose is associated with real harm (Bandolier 122). We now have clarity. The bottom line is that in people without previous cancer, low dose aspirin has no effect over cancer development.

Study [1]

A large number of female healthcare professionals who were at least 45 years old and without previous history of cancer, cardiovascular disease, or other major chronic illness formed the initial cohort. These were randomised to 100 mg aspirin every second day, or placebo. They had not to be taking aspirin or NSAIDs regularly. Enrolment was between mid 1992 to mid 1995, and the end of the trial was in 2004.

Every six months initially, and then annually, participants were sent questionnaires asking about compliance, adverse events, occurrence of endpoints, and risk factors. If an endpoint was reported, medical records were sought and reviewed by a panel of assessors blinded to treatment assignment. Only confirmed cancer endpoints were used.

Results

Just fewer than 40,000 women were randomised. Follow up on morbidity and mortality was close to 100%, and compliance averaged 73%. Women had an average age of 55 years, a mean BMI of 26, and about 13% smoked. About 18% had a family history of cancer. Treatment groups were identical at baseline.

Taking aspirin had no effect on cancer rates, in total or by individual cancer, or cancer type, or on cancer deaths, or on all-cause mortality. No difference was found for any subgroup, for instance those with a family history of cancer, or who smoked.

Over the average 10.1 years of follow up, 2,865 women developed cancer, a rate of just over 7%, or 1 in 14 women (Table 1). About 3% of women died over the 10 years, about 1 in 32, and under half, about 1 in 68, were cancer deaths.

The most common cancers were breast cancer (in 3%), colorectal (0.7%), uterine (0.6%) and lung (0.5%). All other cancers occurred in under half of one percent of women. The overall individual risk of developing a particular cancer over 10 years ranged from 1 in 32 for breast cancer to 1 in 5600 for oesophageal cancer.

Comment

This is an important trial because it tests an important hypothesis in a large number of women over a long period of time, and with a sufficient number of events to be sure of the result. In people with no history of cancer, low-dose aspirin does not prevent cancer. Low dose aspirin is not without harm, however, so on balance in these patients it probably does more harm than good.

Another reason it is important is because it demonstrates that however many observational studies may have sug-

Table 1: Ten-year risk of cancer in female healthcare professionals of average age 55 years (all women in trial)

	Number of women	Percent	10-year risk
Total cancers	2865	7.18	14
Total cancer deaths	583	1.46	68
Total deaths	1251	3.14	32
Individual cancer by site			
Breast	1230	3.08	32
Colorectal	269	0.67	147
Uterine	224	0.56	176
Lung	205	0.51	193
Other sites	151	0.38	262
Melanoma	138	0.35	286
Non-Hodgkin lymphoma	133	0.33	297
Ovary	129	0.32	306
Leukaemia	61	0.15	647
Kidney	61	0.15	647
Thyroid	60	0.15	658
Pancreas	51	0.13	774
Bladder	51	0.13	774
Brain	31	0.08	1274
Multiple myeloma	30	0.08	1316
Stomach	20	0.05	1974
Hodgkin lymphoma	11	0.03	3589
Oesophagus	7	0.02	5640

gested there was a connection between aspirin or NSAID consumption and lower rates of cancer, they were almost certainly wrong. Whatever was going on, it wasn't the aspirin or NSAID causing lower cancer rates.

It may be that higher aspirin doses might have some effect, and here the dose was only 50 mg a day on average. It may be that inhibition of different cyclooxygenase enzymes (cox-2 rather than cox-1) may have an effect, but there is controversy about this because cox-2 inhibition and aspirin caused heart attacks or strokes in polyp prevention studies.

The lesson for all of us is that however good an observational study may be, it can still be wrong, especially in complex situations where there is limited effect and possible unknown confounding factors.

Reference:
1 NR Cook et al. Low-dose aspirin in the primary prevention of cancer. JAMA 2005 294: 47-55.

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Click to get sick?

It is all too easy to make mistakes, and most of us spend a lot of time making sure that mistakes are minimised. It is called quality control, the art of finding out how bad you are.

Cochrane disaster

Two papers [1,2] chart the course of a Cochrane review that was wrong. The review concerned computer or web-based packages for patients, intended to change behaviour. It was published, criticised, and then withdrawn, when it was realised that the main conclusions were the wrong way round. It wrongly claimed that such interventions were bad for patients. Some main criticisms were:

- Results were reversed in 8 of 11 studies
- Three studies contributing most to the negative result were in fact positive
- Not all available studies had been included, but were in previously available systematic reviews

It was likely that the complexity of computer analysis systems used contributed to the mistake, but it was not spotted by authors, peer reviewers, or editors.

Power of the press release

A press release saying that knowledge may be hazardous to web consumers' health compounded the mistake. It was picked up by the mass media, and appeared in many websites and newspapers, and on television and radio. The retraction was not picked up, and the majority of internet citations to the original publication did not mention the retraction [1].

Comment

Much of what we see in the media is generated by press releases. Most journalists do not look beyond the press release. They simply don't have the time to do so, or (often) the skill to do so. Few people read research beyond the abstract, and so the press release effectively determines what we hear.

So mistakes are made. Bandolier reads too much to be surprised by that. But those who are surprised, or who want to read the exceptionally insightful analyses in detail, just dial up the Journal of Medical Internet Research (www.jmir.org). You'll learn a lot and have a few prize illusions shattered.

For the record, the overwhelming evidence is that computer or web-based information systems for patients do much more good than harm.

References:
1 R Rada. A case study of a retracted systematic review on interactive health communication applications: impact on media, scientists, and patients. Journal of Medical Internet Research 2005 7:e18.
2 G Eysenbach, PE Kummervold. "Is cybermedicine killing you?" – the story of a Cochrane disaster. Journal of Medical Internet Research 2005 7:e21.